Notice of Allowability	Application No.	Applicant(s)	
	08/758,033	CLAYMAN, GARY L.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *7/29/2005*.

2. ☒ The allowed claim(s) is/are *1-9, 11-14, 16-20, 26-32, 36, 37 and 146-150*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

This application filed November 27, 1996, claims benefit to provisional application 60/007,810, filed November 30, 1995.

The appeal brief filed July 29, 2005, has been received and entered.

Claims 1-9, 11-14, 16-20, 26-32, 36, 37 and 146-150 are pending and currently under examination.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14, 16-20, 26-32, 36, 37 and 146-150 provisionally rejected under the judicially created doctrine of double patenting over claims 26-88 of copending Application No. 09/968,958 is withdrawn.

In this case, the present application is the senior application of the two, and first to set forth allowed claims. Since it is a provisional rejection, the rejection is withdrawn.

Previously, it was noted that should claim 1 be found allowable, claim146 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. It was argued that simply indicating the mechanism on how the method works does not distinguish the claimed method of 146 from that set forth in claim 1.

Applicants have not addressed this objection in previous arguments nor in the appeal brief. However, upon reconsideration Examiner would note that the skilled artisan could practice the same method steps and result in materially different outcomes as set forth in the preamble of the two claims. More specifically, depending on the specific cell type to which the viral vector is delivered and the amount of expression of p53 in a given cell, the ultimate affect could be inhibition of cell growth or apoptosis. In this case, the scope of the claims are not equivalent as indicated by the preamble of the claim.

Response to Amendment

Applicant notes that the declaration filed June 13, 2002 (attached to comments regarding the decision from the BPAI), and the statement of Dr. Clayman supports that the invention was conceived and due diligence followed that antedates the November 1995 date of the cited references. See applicant's appeal brief, page 8. Applicant's arguments have been considered, and found persuasive.

The details of the information regarding applications for FDA trials and Grand Rounds seminar are sufficient evidence that the claimed invention was conceived prior to the publication of both Katayose and Srivastava references.

Claim Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9, 13, 14, 16-20 and 36 rejected under 35 U.S.C. 102(b) as being anticipated by Liu *et al.* (IDS Reference) is withdrawn.

Applicant notes that Liu *et al.* teaches the method in an animal model, not for the treatment of humans as instantly claimed.

Examiner agrees with Applicants summary of the teaching of Liu *et al.*

Claims 1-9, 13, 14, 16-20 and 36 rejected under 35 U.S.C. 102(a) as being anticipated by Clayman *et al.* is withdrawn.

Review of the declaration provided in Exhibit J demonstrates that the Clayman *et al.* reference is not by another, therefore does not qualify as a 102(a) type reference.

Claims 1-14, 16-20, 26-32, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Roth *et al.* (5,747,469 or 6,017,524) is withdrawn.

Examiner agrees with Applicants summary of the teaching of Roth *et al.*

Claims 1-14, 16-20, 26-32, 36, 37 146, 148 and 150 rejected under 35 U.S.C. 102(b) as being anticipated by Roth *et al.* (6,069,134) is withdrawn.

Claims 1-14, 16-20, 26-32, 36 and 37 rejected under 35 U.S.C. 102(b) as being anticipated by Vogelstein *et al.* (6,677,312) is withdrawn.

Applicants argue that neither Roth *et al.* (6,069,134) nor Vogelstein *et al.* (6,677,312) specifically teach to practice the method as claimed. More specifically, it is noted that all the working examples and general guidance in the art at the time of filing focused on replacing a mutant form of p53, not on expressing p53 in cells that express a normal p53 as recited and encompassed by the instant claims (see for example the preamble of claim 1). Applicants'

arguments have been fully considered and found persuasive. Examiner agrees that while both references teach to provide p53 to kills cells in the treatment of cancer, neither specifically teach to use the strategy on a cell that expresses p53.

Claim Rejections - 35 U.S.C. 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14, 16-20, 26-32, 36 and 37 rejected under 35 U.S.C. 103(a) as being unpatentable over Clayman *et al.* and Liu *et al.* in view of Zhang *et al.* is withdrawn.

Since the teaching of Clayman *et al.* is not by another, the combined teaching fail to teach all of the limitations set forth in the claims.

Claims 1-14, 16-20, 26-32, 36, 37 and 146-150 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava *et al.*, Cajot *et al.*, Katayose *et al.*, Will *et al.*, Liu *et al.* and Zhang *et al.* is withdrawn.

As noted above, the declaration of Dr. Clayman was sufficient to obviate the use of either Srivastava *et al.* or Katayose *et al.* in the rejection. Without the teachings of these two references the rejection fails to meet the requirements of making a rejection under 35 USC 103.

Claims 1-14, 16-20, 26-32, 36, 37, 146-150 are rejected under 35 U.S.C. 103 as being unpatentable over Roth *et al.* (6,069,134), Liu *et al.*, Vogelstein *et al.* (6,677,312) in view of Baker *et al.* (Science 249(4971):912-915, Aug 24, 1990) and Shaw *et al.* (PNAS 89:4495-4499, May 1992) is withdrawn.

Applicants note that Roth *et al.* is not available as prior art. Further, Applicants argue that the references provided fail to anticipate the claimed invention, and evidence provided teaches away from the invention as claimed. Examiner agrees with Applicants' overall arguments. The essential issue regarding Applicants arguments throughout the prosecution has been that the cited art fails to teach the administration of a functional p53 to cells that already express p53. Examiner agrees that the prior art at the time of filing focused on treating cancer by providing a functional copy of p53 to cells that did not express p53 or expressed mutant forms of p53. It has been argued that there is no motivation nor expectation of success that administering p53 to cells that already have and express a functional p53 would have any affect in treating cancer, more specifically in the inhibition of tumor growth. The Examiner provided secondary references to demonstrate that at least *in vitro*, the art taught that transformed cells containing a functional p53 could be affected when p53 was over-expressed as a transgene in the cell. Applicants have reviewed the cited references and noted that Baker *et al.* teach that VACO 235 cells that have functional alleles are not affected by wild-type p53 expression (appeal brief, page 8). With respect to the teachings of Shaw *et al.* Applciants note the teaching of the affect of p53 on cell cycle regulation, however the reference fails to teach what affect p53 expression would be when normal endogenous levels of p53 are present in the cell (appeal brief, page 9). The cited primary references primarily teach to treat cancer by expressing p53 to correct p53, *i.e.*

in cells that fail to express or express mutated forms of p53, and lack of specific teaching to treat cells with normal p53 expression. The teaching of treating cells with altered p53, bolstered by the fact that the teachings of the secondary references teach some cells with normal p53 alleles are not affected by exogenous p53 expression *in vitro*, the references of record fail to anticipate each of the limitations of the claimed invention, and provide no specific expectation of success for the invention as claimed.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

At the time of filing, the art teaches the administration of viral vectors expressing p53 to treat cancer, however the treatment was directed to cancers where p53 was mutated or had altered expression in order to correct the normal function of p53 in a given cell. Further, at the time of filing the role of p53 in cell cycle control was well studied, in particular in the apparent requirement of p53 to stop cell cycle progression at various check-points in the cell cycle. The present specification is the first to provide evidence that over-expression of exogenous p53 in some cell types results in reduced growth and sometimes cell death through the apoptotic pathway. Moreover, the present disclosure has provided *in vivo* evidence of phase I trials that support the fact that *in vitro* observations of cells in culture are applicable to *in vivo* treatments of a tumor in a subject.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue

fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach